

**REMARKS**

Claims 22, 23, 28, 29 and 43 have been amended. Support for the amendments can be found throughout the present specification, for example, at page 6, lines 12-23. Claim 42 has been canceled without prejudice or disclaimer.

Claims 22-41 and 43 are pending in the application, with claims 22, 28, 29 and 43 being the independent claims.

**I. The Objection to Claim 29 Has Been Rendered Moot**

In the Office Action at page 2, claim 29 and its dependent claims have been objected to for allegedly being of improper dependent form for failing to further limit the subject matter of a previous claim. The Office action contends that, since apparatus claim 29 could be infringed on by an apparatus that does not necessarily involve the method steps of claim 22, then the claim fails to satisfy the infringement test. Applicants respectfully traverse this objection and disagree with these contentions.

However, solely to expedite prosecution and not in acquiescence to this objection, present claim 29 has been re-written as an independent claim. Hence, this objection has been rendered moot.

**II. The Double Patenting Objection Has Been Rendered Moot**

In the Office Action at page 3, it has been asserted that should claim 42 be found allowable, claim 23 will be objected to as allegedly being a substantial duplicate thereof. Applicants respectfully traverse this objection and disagree with these contentions.

However, solely to expedite prosecution and not in acquiescence to this objection, claim 42 has been canceled. Hence, this objection has been rendered moot.

**III. The Rejection of Claims 22 and 28 Under 35 U.S.C. § 103 Should be Withdrawn**

Claims 22 and 28 have been rejected under 35 U.S.C. § 103(a), as allegedly being unpatentable over U.S. Patent No. 6,280,703 to Combs *et al.* (hereafter "Combs"), in view of U.S. Patent No. 4,969,175 to Nelson *et al.* (hereafter "Nelson"). Applicant respectfully traverses this rejection.

The Office Action suggests that Combs discloses an imaging method comprising simultaneously determining *in vivo* distributions of bioluminescent and/or fluorescent markers and radioactive markers utilizing a first and second detector. The Office Action indicates that Combs discloses that the first and second detectors are arranged in a specific spatial arrangement relative to each other.

The Office Action concedes, however, that Combs fails to disclose that the detectors are placed at identical projection angles, and relies on the disclosure of Nelson to cure this deficiency. Specifically, the Office Action suggests that Nelson, in the field of multiple energy x-ray imaging, discloses imaging at two different energy levels at the same projection angle. The Office Action concludes that it would have been obvious to determine the distributions of the markers at the same projection angle in order to properly compare the detected energies relative to the part being imaged. Applicant respectfully disagrees with these contentions and conclusions.

Applicant respectfully submits that, contrary to the assertions in the Office Action, Combs does not disclose an imaging method as set forth in the presently claimed invention. Specifically, Combs does not disclose a method of claim 22 comprising simultaneously determining *in vivo* distributions of bioluminescent and/or fluorescent markers and radioactive markers at identical projection angles, and reconstructing an image of the distribution of the markers following the determining, or a method of claim 28 comprising alternately determining *in vivo* distributions of bioluminescent and/or fluorescent markers and *in vivo* distributions of radioactive markers with a common measurement apparatus, and reconstructing an image of the distribution of the markers following the determining.

Combs is directed to detection of the presence of "tracers" in a body fluid. *See* Combs at column 5, lines 14-16. ("The detection of the tracers can be achieved by radiometric, magnetic,

ultrasonic, or optical methods known in the art.”) Applicant submits that a person of ordinary skill in the art would clearly understand that a method of *detecting* the signal from a tracer is not the same as the presently claimed methods of imaging that require reconstructing an image of the distribution of the markers following the determining.

Simply because Combs discloses that its methods are capable of “assessing organ function” by detecting the signal from a tracer in a body fluid, there is no indication that an image of the distribution of the signals is or could be reconstructed. The data generated by the method of Combs simply provides a time course of signal intensity values. *See, e.g.*, Combs at Figures 2-4. Combs provides no image (i.e., a 2-dimensional or 3-dimensional picture) reconstructed from the signals.

Applicant submits that this deficiency in Combs is not cured by the disclosure of Nelson. Simply because Nelson may disclose X-ray imaging utilizing two different X-ray energy levels, there is no indication that Nelson could be combined with Combs in order to generate a method where the signals detected by Combs are reconstructed as an image of the distribution of the signals. Nelson relates to imaging utilizing two different X-ray energy levels, not photons from bioluminescent and/or fluorescent markers having a first average energy *and* photons from radioactive markers having a second average energy, as recited in the presently claimed invention.

Applicant submits that, contrary to the assertions in the Office Action, there would not have been a reasonable expectation of success that methods of detecting two different x-ray energy levels could be utilized to detect energy emitted by bioluminescent and/or fluorescent markers and also separate energy from photons from radioactive markers. Nelson provides no indication that the disclosed methods could be utilized for anything beyond x-ray imaging. As set forth in M.P.E.P. § 2143.02, absent a reasonable expectation of success, a *prima facie* case of obviousness cannot be established.

In response to Applicant’s arguments submitted with the Reply to Office Action dated September 24, 2010, the Office Action contends that the previous claims merely recited “imaging” in the preamble, and provided no positive recitation of imaging steps. Applicants respectfully disagree. However, solely to expedite prosecution, the presently claimed methods

clearly recite the step of “reconstructing an image of the distribution of the markers following the determining.” Applicant submits that this clearly sets forth a positive step in the presently claimed methods that directly provides for the generation of an image.

Applicant respectfully submits that the Examiner has not set forth a proper *prima facie* case of obviousness. In view of the foregoing remarks, Applicant respectfully requests reconsideration and withdrawal of the rejection under 35 U.S.C. § 103(a).

**IV. The Rejection of Claims 23, 24, 42 and 43 Under 35 U.S.C. § 103 Should be Withdrawn**

Claims 23, 24, 42 and 43 have been rejected under 35 U.S.C. § 103(a), as allegedly being unpatentable over Combs in view of Nelson and further in view of U.S. Patent No. 6,757,554, to Rubinstein, et al. (hereinafter “Rubinstein”). Applicants note that the Office Action referred to claims 43 and 44 in the rejection. However, it appears that claims 42 and 43 were intended. Claim 42 has been canceled. Hence, this rejection has been rendered moot as it may have applied to this claim. Applicant respectfully traverses this rejection as it may apply to the remaining claims.

The Office Action suggests that Combs and Nelson disclose the claimed invention as set forth above. However, the Office Action concedes that the combination of Combs and Nelson fails to disclose a layer used to transmit or reflect photons according to their energy level. The Office Action attempts to cure this deficiency with the disclosure of Rubinstein, suggesting that Rubinstein discloses a filter. The Office Action concludes that it would have been obvious to provide a layer for each of the detectors in order to minimize background emissions and only allow the intended range of emission energies to pass. Applicant respectfully disagrees with these contentions and conclusions.

As set forth above, Applicant submits that Combs and Nelson do not disclose the presently claimed invention, as the combination of references fails to disclose the presently claimed methods of imaging. Applicant submits that this deficiency is not cured by the disclosure of Rubinstein, as Rubinstein also does not disclose a method of imaging, let alone a

method wherein the distribution of the bioluminescent and/or fluorescent markers is determined by separate detection of photons having a first average energy, which are emitted by the bioluminescent and/or fluorescent markers, by at least one first detector and wherein the distribution of the radioactive markers is determined by simultaneous separate detection of photons having a second average energy, which are emitted by the radioactive markers, by at least one second detector, and reconstructing an image of the distribution of the markers following the determining.

Applicant notes that if an independent claim is nonobvious under 35 U.S.C. § 103, then any claim depending therefrom is nonobvious. *In re Fine*, 5 USPQ2d 1596 (Fed. Cir. 1988). *See* M.P.E.P. § 2143.03. Thus, Applicants submit that as claim 22 is nonobvious, claims 23 and 24, each of which ultimately depends from independent claim 22, are also non-obvious at least by virtue of their dependency from claim 22.

Furthermore, present claims 23 (and hence, claim 24 that depends ultimately therefrom), and claim 43, recite that in the step of determining in vivo distributions, the photons of the bioluminescent and/or fluorescent markers having the first average energy and the photons of the radioactive markers having the second average energy are separated for the separate detection with the aid of a layer, the layer essentially reflecting the photons of the bioluminescent and/or fluorescent markers *and* transmitting the photons of the radioactive marker. Contrary to the suggestions in the Office Action, Applicant asserts that the filter disclosed in Rubinstein is utilized to filter out specific wavelengths of light. *See* Rubinstein at column 8, lines 48-50. There is no indication in Rubinstein that such filters would or even could reflect the photons of the bioluminescent and/or fluorescent markers *and also* transmit the photons of the radioactive markers.

In response to Applicant's arguments submitted with the Reply to Office Action dated September 24, 2010, the Office Action contends that one of ordinary skill in the art would understand that the filter is an obvious solution for the selective separation of the different photon energies to their respective detectors. However, Applicant submits that there is no indication that the filter disclosed in Rubinstein reflects the photons of the bioluminescent and/or fluorescent markers *and* transmits the photons of the radioactive markers. The filters disclosed

in Rubinstein are specifically designed to “minimize the background of the [fluorescent] emission signals detected.” Rubinstein at column 8, lines 45-50. Thus, the filters of Rubinstein in fact allow *transmission* of particular photons of fluorescent markers, while absorbing others that are not allowed to pass. They do not *reflect* these photons, as required in the presently claimed invention.

Applicant respectfully submits that the Examiner has not set forth a proper *prima facie* case of obviousness. In view of the foregoing remarks, Applicant respectfully requests reconsideration and withdrawal of the rejection under 35 U.S.C. § 103(a).

**V. The Rejection of Claim 25 Under 35 U.S.C. § 103 Should be Withdrawn**

Claim 25 has been rejected under 35 U.S.C. § 103(a), as allegedly being unpatentable over Combs in view of Nelson and further in view of U.S. Patent No. 6,232,107, to Bryan, *et al.* (hereinafter “Bryan”). Applicant respectfully traverses this rejection.

The Office Action suggests that Combs and Nelson disclose the present invention as set forth above. However, the Office Action concedes that the combination of Combs and Nelson fails to disclose the use of green fluorescent proteins (GFP). The Office Action attempts to cure this deficiency with the disclosure of Bryan, suggesting that Bryan discloses GFP. The Office Action concludes that it would have been obvious to utilize GFP in the combined method of Combs and Nelson. Applicant respectfully disagrees with these contentions and conclusions.

As set forth above, Applicant submits that Combs and Nelson do not disclose the presently claimed invention, as the combination of references fails to disclose the presently claimed methods of imaging. Applicant submits that this deficiency is not cured by the disclosure of Bryan, as Bryan also does not disclose a method of imaging, let alone a method wherein the distribution of the bioluminescent and/or fluorescent markers is determined by separate detection of photons having a first average energy, which are emitted by the bioluminescent and/or fluorescent markers, by at least one first detector and wherein the distribution of the radioactive markers is determined by simultaneous separate detection of photons having a second average energy, which are emitted by the radioactive markers, by at

least one second detector, and reconstructing an image of the distribution of the markers following the determining.

Applicant notes that if an independent claim is nonobvious under § 103, then any claim depending therefrom is nonobvious. *In re Fine*, 5 USPQ2d 1596 (Fed. Cir. 1988). See M.P.E.P. § 2143.03. Thus, Applicant submits that as claim 22 is nonobvious, claim 25, which ultimately depends from independent claim 22, is also non-obvious at least by virtue of its dependency from claim 22. Applicant respectfully submits that the Examiner has not set forth a proper *prima facie* case of obviousness. In view of the foregoing remarks, Applicant respectfully requests reconsideration and withdrawal of the rejection under 35 U.S.C. § 103(a).

#### **VI. The Rejection of Claim 26 Under 35 U.S.C. § 103 Should be Withdrawn**

Claim 26 has been rejected under 35 U.S.C. § 103(a), as allegedly being unpatentable over Combs in view of Nelson and further in view of Published U.S. Patent Application No. 2003/0101466, to Turner (hereinafter “Turner”). Applicant respectfully traverses this rejection.

The Office Action suggests that Combs and Nelson disclose the present invention as set forth above. However, the Office Action concedes that the combination of Combs and Nelson fails to disclose detecting Indium-111 using SPECT. The Office Action attempts to cure this deficiency with the disclosure of Turner, suggesting that Turner discloses the use of SPECT to detect Indium-111. The Office Action concludes that it would have been obvious to utilize Indium-111 in the combined method of Combs and Nelson. Applicant respectfully disagrees with these contentions and conclusions.

As set forth above, Applicant submits that Combs and Nelson do not disclose the presently claimed invention, as the combination of references fails to disclose the presently claimed methods of imaging. Applicant submits that this deficiency is not cured by the disclosure of Turner, as Turner also does not disclose a method of imaging, let alone a method wherein the distribution of the bioluminescent and/or fluorescent markers is determined by separate detection of photons having a first average energy, which are emitted by the

bioluminescent and/or fluorescent markers, by at least one first detector and wherein the distribution of the radioactive markers is determined by simultaneous separate detection of photons having a second average energy, which are emitted by the radioactive markers, by at least one second detector, and reconstructing an image of the distribution of the markers following the determining.

Applicant notes that if an independent claim is nonobvious under § 103, then any claim depending therefrom is nonobvious. *In re Fine*, 5 USPQ2d 1596 (Fed. Cir. 1988). *See* M.P.E.P. § 2143.03. Thus, Applicant submits that as claim 22 is nonobvious, claim 26, which ultimately depends from independent claim 22, is also non-obvious at least by virtue of its dependency from claim 22. Applicant respectfully submits that the Examiner has not set forth a proper *prima facie* case of obviousness. In view of the foregoing remarks, Applicant respectfully requests reconsideration and withdrawal of the rejection under 35 U.S.C. § 103(a).

## **VII. The Rejection of Claim 27 Under 35 U.S.C. § 103 Should be Withdrawn**

Claim 27 has been rejected under 35 U.S.C. § 103(a), as allegedly being unpatentable over Combs in view of Nelson and further in view of Turner and U.S. Patent No. 6,312,961, to Voirin et al. (hereinafter “Voirin”). Applicant respectfully traverses this rejection.

The Office Action suggests that Combs, Nelson and Turner disclose the present invention as set forth above. However, the Office Action concedes that the combination of Combs, Nelson and Turner fail to disclose detecting fluorescent markers using a CCD camera. The Office Action attempts to cure this deficiency with the disclosure of Voirin, suggesting that Voirin discloses the use of a CCD camera to detect fluorescent emissions. The Office Action concludes that it would have been obvious to utilize CCD camera to detect fluorescent emissions in the combined method of Combs, Nelson and Turner. Applicant respectfully disagrees with these contentions and conclusions.

As set forth above, Applicant submits that Combs, Nelson and Turner do not disclose the presently claimed invention, as the combination of references fails to disclose the presently



claimed methods of imaging. Applicant submits that this deficiency is not cured by the disclosure of Voirin, as Voirin also does not disclose a method of imaging, let alone a method wherein the distribution of the bioluminescent and/or fluorescent markers is determined by separate detection of photons having a first average energy, which are emitted by the bioluminescent and/or fluorescent markers, by at least one first detector and wherein the distribution of the radioactive markers is determined by simultaneous separate detection of photons having a second average energy, which are emitted by the radioactive markers, by at least one second detector, and reconstructing an image of the distribution of the markers following the determining.

Applicant notes that if an independent claim is nonobvious under § 103, then any claim depending therefrom is nonobvious. *In re Fine*, 5 USPQ2d 1596 (Fed. Cir. 1988). See M.P.E.P. § 2143.03. Thus, Applicants submit that as claim 22 is nonobvious, claim 27, which ultimately depends from independent claim 22, is also non-obvious at least by virtue of its dependency from claim 22. Applicant respectfully submits that the Examiner has not set forth a proper *prima facie* case of obviousness. In view of the foregoing remarks, Applicant respectfully requests reconsideration and withdrawal of the rejection under 35 U.S.C. § 103(a).

#### **VIII. The Rejection of Claims 29 and 30 Under 35 U.S.C. § 103 Should be Withdrawn**

Claims 29 and 30 have been rejected under 35 U.S.C. § 103(a), as allegedly being unpatentable over Combs in view of Nelson and further in view of Turner, Voirin and Rubinstein. Applicant respectfully traverses this rejection.

The Office Action suggests that Combs, Nelson, Turner and Voirin disclose the present invention as set forth above. However, the Office Action concedes that the combination of Combs, Nelson, Turner and Voirin fails to disclose the use of a layer to transmit or reflect photons according to their energy level. The Office Action attempts to cure this deficiency with the disclosure of Rubinstein, suggesting that Rubinstein discloses a filter. The Office Action concludes that it would have been obvious to utilize the filter of Rubinstein in the combined method of Combs, Nelson, Turner and Voirin. Applicant respectfully disagrees with these contentions and conclusions.

Applicants respectfully submit that the combination of Combs, Nelson, Turner, Voirin and Rubinstein fail to disclose the presently claimed apparatus set forth in claim 29, specifically an apparatus comprising a layer which essentially reflects the photons of the bioluminescent and/or fluorescent markers to a CCD camera *and* essentially transmits the photons of the radioactive markers to a SPECT detector.

As discussed in detail above, the filter disclosed in Rubinstein is essentially a band-pass filter which minimizes “the background of the emission signals detected.” *See* Rubinstein at column 8, lines 45-50. There is no disclosure of a layer in Rubinstein, which essentially reflects the photons of the bioluminescent and/or fluorescent markers to a CCD camera *and also* essentially transmits the photons of the radioactive markers to a SPECT detector. In fact, there is no mention that the filter disclosed in Rubinstein reflects any types of signals. Applicants therefore submit that the Office Action has not set forth a proper *prima facie* case of obviousness.

Applicant notes that if an independent claim is nonobvious under § 103, then any claim depending therefrom is nonobvious. *In re Fine*, 5 USPQ2d 1596 (Fed. Cir. 1988). *See* M.P.E.P. § 2143.03. Thus, Applicants submit that as claim 29 is nonobvious, claim 30, which ultimately depends therefrom is also non-obvious at least by virtue of its dependency from claim 30. Applicant respectfully submits that the Examiner has not set forth a proper *prima facie* case of obviousness. In view of the foregoing remarks, Applicant respectfully requests reconsideration and withdrawal of the rejection under 35 U.S.C. § 103(a).

**IX. The Rejection of Claims 31-34 and 36-41 Under 35 U.S.C. § 103 Should be Withdrawn**

Claims 31-34 and 36-41 have been rejected under 35 U.S.C. § 103(a), as allegedly being unpatentable over Combs in view of Nelson and further in view of Turner, Voirin, Rubinstein and further in view of U.S. Patent No. 5,647,363 to Rabito et al. (hereinafter “Rabito”). Applicant respectfully traverses this rejection.

The Office Action suggests that Combs, Nelson, Turner, Voirin and Rubinstein disclose the present invention as set forth above. However, the Office Action concedes that the combination of Combs, Nelson, Turner, Voirin and Rubinstein fails to disclose the different configurations and arrangements of the SPECT and CCD cameras. The Office Action attempts to cure this deficiency with the disclosure of Rabito, suggesting that Rabito discloses the recited arrangement.

As set forth above, Applicant submits that Combs, Nelson, Turner, Voirin and Rubinstein do not disclose the presently claimed invention, as the combination of references fails to disclose the presently claimed apparatus set forth in claim 29, specifically an apparatus comprising a layer which essentially reflects the photons of the bioluminescent and/or fluorescent markers to a CCD camera and essentially transmits the photons of the radioactive markers to a SPECT detector.

Applicant submits that this deficiency is not cured by the disclosure of Rabito, as Rabito also does not disclose a layer which essentially reflects the photons of the bioluminescent and/or fluorescent markers to a CCD camera and essentially transmits the photons of the radioactive markers to a SPECT detector.

Applicant notes that if an independent claim is nonobvious under § 103, then any claim depending therefrom is nonobvious. *In re Fine*, 5 USPQ2d 1596 (Fed. Cir. 1988). See M.P.E.P. § 2143.03. Thus, Applicant submits that as claim 29 is nonobvious, claims 31-34 and 36-41, which ultimately depend from independent claim 29, are also non-obvious at least by virtue of their dependency from claim 29. Applicant respectfully submits that the Examiner has not set forth a proper *prima facie* case of obviousness. In view of the foregoing remarks, Applicant respectfully requests reconsideration and withdrawal of the rejection under 35 U.S.C. § 103(a).

**X. The Rejection of Claim 35 Under 35 U.S.C. § 103 Should be Withdrawn**

Claim 35 has been rejected under 35 U.S.C. § 103(a), as allegedly being unpatentable over Combs in view of Nelson and further in view of Turner, Voirin, Rubinstein, Rabito and

further in view of Published U.S. Patent Application No. 2002/0042566 to Matsuzaki *et al.* (hereinafter “Matsuzaki”). Applicant respectfully traverses this rejection.

The Office Action suggests that Combs, Nelson, Turner, Voirin, Rubinstein and Rabito disclose the present invention as set forth above. However, the Office Action concedes that the combination of Combs, Nelson, Turner, Voirin, Rubinstein and Rabito fails to disclose the use of a position sensor. The Office Action attempts to cure this deficiency with the disclosure of Matsuzaki, suggesting that Matsuzaki discloses the use of a positions sensor.

As set forth above, Applicant submits that Combs, Nelson, Turner, Voirin, Rubinstein and Rabito do not disclose the presently claimed invention, as the combination of references fails to disclose the presently claimed apparatus set forth in claim 29, specifically an apparatus comprising a layer which essentially reflects the photons of the bioluminescent and/or fluorescent markers to a CCD camera and essentially transmits the photons of the radioactive markers to a SPECT detector.

Applicant submits that this deficiency is not cured by the disclosure of Matsuzaki, as Matsuzaki also does not disclose a layer which essentially reflects the photons of the bioluminescent and/or fluorescent markers to a CCD camera *and also* essentially transmits the photons of the radioactive markers to a SPECT detector.

Applicant notes that if an independent claim is nonobvious under § 103, then any claim depending therefrom is nonobvious. *In re Fine*, 5 USPQ2d 1596 (Fed. Cir. 1988). See M.P.E.P. § 2143.03. Thus, Applicants submit that as claim 29 is nonobvious, claim 35, which ultimately depends from independent claim 29, is also non-obvious at least by virtue of its dependency from claim 29. Applicant respectfully submits that the Examiner has not set forth a proper *prima facie* case of obviousness. In view of the foregoing remarks, Applicant respectfully requests reconsideration and withdrawal of the rejection under 35 U.S.C. § 103(a).

**XI. Conclusion**

Applicant believes that the currently pending claims are allowable and respectfully request allowance thereof. The Examiner is invited to telephone the undersigned if that would be helpful to resolving any issues.

It is believed no additional fees beyond those provided herewith are due; however, the commissioner is authorized to charge any fees and credit any overpayments to Deposit Account No. 50-5071 which may be due.

Respectfully submitted,

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By: /Paul D. Strain/

FANELLI, STRAIN & HAAG PLLC  
**Customer No. 0091436**  
1455 Pennsylvania Avenue, N.W.  
Suite 400  
Washington, D.C. 20004  
Telephone: 202.621.1840  
Facsimile: 202.621.1844

Paul D. Strain  
Registration No. 47,369  
Attorney for Applicant  
  
Jeffrey K. Mills  
Registration No. 56,413  
Attorney for Applicant